clarify what Applicants regard as their invention. In particular, claims 20, 21, 29, 30, 48, 49 and 50 have been amended to replace the term "subject" with the term "animal". Claims 21 and 30 have been further amended such that they no longer depend from claim 58 or 59 and claim 60, respectively. New claim 62 has been added to depend from claims 58-60 and recites that the animal in which the cancer is detected in accordance with the claimed methods is a human. A marked up version of the claims showing the amendments to claims 20, 21, 29, 30, 48, 49, and 50, with deletions and additions indicated by brackets and underlining, respectively, is attached hereto as Exhibit A. Support for the amendments to claims 20, 21, 29, 30, 48, 49, and 50 and new claim 62 can be found throughout the present application, see, *e.g.*, page 39, line 20 to page 40, line 22 of the present specification. Applicants assert that the amendments to 20, 21, 29, 30, 48, 49, and 50 and new claim 62 do not constitute new matter. Claims 20-24, 26-34, 48-53, 55, 56 and 58-62 are, therefore, pending in the present application. A copy of the pending claims is attached hereto as Exhibit B.

Applicants respectfully request entry of the foregoing amendments and remarks into the file history of the above-identified application.

1. INTERVIEW SUMMARY RECORD

Applicants and Applicants' representatives thank Examiner Karen Canella for the courtesy of reviewing the claim rejections under 35 U.S.C. § 112, second paragraph, in the present Office Action, in connection with the above-identified application. Upon review of the claim rejections under 35 U.S.C. § 112, second paragraph, in the present Office Action, Examiner Canella in a voice message to Applicants' representative Geraldine F. Baldwin on January 23, 2002 stated that she was not going to maintain the claim rejections under 35 U.S.C. § 112, second paragraph.

2. THE REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH, SHOULD BE WITHDRAWN

Claims 58-61 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. The Office Action alleges that "[c]laims 58-61 fail to relate the administration of one or more antibodies known to bind to improperly glycosylated

cancer cells in a subject to the detection of cancer in a subject as only the detection of anti-C3bi antibody label is related to the presence of cancer." For the reasons detailed below, the rejection cannot stand and should be withdrawn.

"The test for definiteness is whether one skilled in the art would understand the bounds of the claim when read in light of the specification." *Miles Laboratories, Inc. v. Shandon Inc.* 997 F.2d 870, 875 (Fed. Cir. 1994).

Applicants respectfully assert that one of skill in the art in view of the teachings of the present specification would appreciate that the administration of IgM antibodies, which are known to bind to improperly glycosylated cancer cells, enhance C3b(i) opsonization and thus, provide unique and specific determinants for targeting by antibodies which specifically bind to C3b(i) (see, *e.g.*, page 9, lines 24-26 of the instant specification). Thus, Applicants respectfully assert that one of skill in the art would understand the metes and bounds of claims 58-61. Further, as discussed above, the Examiner in a voice message to Applicants' representative Geraldine F. Baldwin on January 23, 2002 stated that she would not maintain the rejection of claims 58-61 under 35 U.S.C. § 112, second paragraph. Accordingly, Applicants respectfully assert that claims 58-61 are definite and the rejection under 35 U.S.C. § 112, second paragraph, cannot stand and should be withdrawn. Therefore, claims 58-61 are in condition for allowance.

3. THE CLAIMED INVENTION IS NOT OBVIOUS

Claims 20-34, 48-53, 55, and 56 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Kinders et al., U.S. Patent No. 6,221,621 ("Kinders") in view of Perlman et al., 1981, Journal of Experimental Medicine 153:1592-1603 ("Perlman") and Michael et al., 1993, FASEB 7:A375 ("Michael"). The Office Action alleges that Kinders describes a method of detecting cancer comprising the detection of C3. The Office Action concedes that Kinders does not teach a method of detecting cancer comprising the detection of C3b(i). However, the Office Action alleges that Perlman teaches that C3b(i) constitutes the largest C3 fragment deposited on target cells and that Michael teaches that malignant epithelial cells synthesize C3b(i). The Office Action alleges that it would have been *prima facie* obvious to one skilled in the art at the time the invention was made to substitute the detection of C3b(i) with the detection of C3 in a method of detecting cancer. For the reasons detailed below, the rejection cannot stand and should be withdrawn.

Applicants have amended claims 20, 21, 29, 30, 48, 49, and 50 to more particularly point out and distinctly claim the subject matter of their invention. In particular, claims 20, 21, 29, 30, 48, 49, and 50 have been amended by replacing the term "subject" with the term "animal".

A finding of obviousness requires a determination of the scope and content of the prior art, the level of ordinary skill in the art, the differences between the claimed subject matter and the prior art, and whether the differences are such that the subject matter as a whole would have been obvious to one of ordinary skill in the art at the time the invention was made. *Graham v. Deere* 383 U.S. 1 (1996). The proper inquiry is whether the art suggests the invention, and whether the art provides one of ordinary skill in the art with a reasonable expectation of success. *In re O'Farrell* 853 F.2d 894, 7 USPQ2d 1673 (Fed. Cir. 1988). Both the suggestion and the reasonable expectation of success must be founded in the prior art and not in the Applicants' disclosure. *In re Vaeck* 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). It is impermissible to engage in hindsight reasoning, using the claims as a frame and the prior art reference as a mosaic to piece together a facsimile of the claimed invention. *W.L. Gore & Assoc., Inc. v. Garlock, Inc.* 220 USPQ 303, 312 (Fed. Cir. 1983).

Neither Kinders, Perlman nor Michael, alone or in combination, teach or suggest the methods of the claimed invention. Kinders describes methods of screening for cancer *in vitro* by detecting the presence of C3 or a C3 related protein (C3rp) in a sample (see, *e.g.*, Kinders at column 4, lines 9-13). Kinders does not teach or suggest methods for determining whether cancer is present at a site in an animal by administering to the animal a labeled antibody which specifically binds to C3b(i) or a labeled antibody which specifically binds to C3b(i) covalently linked to a second molecule and detecting whether the labeled antibody is localized at said site. There is no teaching, suggestion or motivation provided by Kinders to detect cancer *in vivo* by imaging an animal subsequent to the administration of a labeled antibody which specifically binds to C3b(i) or a labeled antibody which specifically binds to C3b(i) covalently linked to a second molecule. Further, Kinders does not teach or suggest detecting cancer by administering plasma to an animal prior to the administration of a labeled antibody which specifically binds to C3b(i).

The deficiencies in Kinders are not cured by Perlman or Michael. Perlman teaches that C3b(i) bound to target cells (*i.e.*, erythocytes) enhances antibody-dependent lymphocyte-mediated cytotoxicity (ADCC). Michael is merely an abstract that describes an observation

that C3b(i) is detectable in the supernatant of *in vitro* cultures of the human cervical carcinoma line HeLa S3. Neither Perlman nor Michael teach or suggest methods for determining that cancer is present at a site in an animal by detecting if a labeled antibody which specifically binds to C3b(i) or a labeled antibody which specifically binds to C3b(i) covalently linked to a second molecule is localized at said site. Further, neither Perlman nor Michael teach or suggest detecting cancer by administering to a subject plasma prior to the administration of a labeled antibody which specifically binds to C3b(i). In fact, neither Perlman nor Michael even teach or suggest antibodies which specifically bind to C3b(i), much less the use of antibodies which specifically bind to C3b(i) in the detection of cancer in an animal. Thus, neither Kinders, Perlman nor Michael, alone or in combination, teach or suggest the methods of the claimed invention.

In view of the foregoing, the rejection under 35 U.S.C. § 103(a) cannot stand and should be withdrawn.

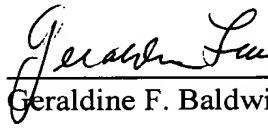
CONCLUSION

Entry of the foregoing amendments and remarks into the file of the above-identified application is respectfully requested. Applicants believe that all of the present claims meet all the requirements for patentability. Withdrawal of all rejections and reconsideration of the amended claims are requested. An allowance is earnestly sought.

If any issues remain, the Examiner is requested to telephone the undersigned at (212) 790-2296.

Respectfully submitted,

Date: April 22, 2001



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Enclosures

EXHIBIT A

A MARKED UP VERSION OF THE CLAIMS AMENDED IN THE AMENDMENT FILED ON APRIL 22, 2002 IN U.S. PATENT APPLICATION SERIAL NO. 09/392,500 ATTORNEY DOCKET NO. 9426-019

20. (Thrice Amended) A method for detecting cancer comprising:

a) administering to an animal an effective amount of a labeled antibody which specifically binds to C3b(i) or a labeled antibody which specifically binds to C3b(i) covalently linked to a second molecule [to a subject];

b) waiting for a time interval following the administration to permit the labeled antibody to concentrate at any cancerous site in the [subject] animal;

c) determining background level;

d) detecting the labeled antibody at a site in the [subject] animal; and

e) determining that cancer is present at said site in the [subject] animal if the labeled antibody is detected above the background level at said site in the [subject] animal.

21. (Thrice Amended) The method of Claim 20, 48[,] or 49, [58 or 59] in which the [subject] animal is a human.

29. (Thrice Amended) A method for detecting cancer in [a subject] an animal, comprising

(a) imaging said [subject] animal at a time interval after administering to said [subject] animal an effective amount of a labeled antibody which specifically binds to C3b(i) or a labeled antibody which specifically binds to C3b(i) covalently linked to a second molecule, said time interval being sufficient to permit the labeled antibody to concentrate at any cancerous site in said [subject] animal; and

(b) determining that cancer is present at a site in said [subject] animal if the labeled antibody is localized at said site in the [subject] animal.

30. (Thrice Amended) The method of Claim 29[,] or 50 [or 60] in which the [subject] animal is a human.

48. (Thrice Amended) A method for detecting cancer comprising:

a) administering plasma to [a subject] an animal;

b) administering an effective amount of a labeled antibody which specifically binds to C3b(i) to said [subject] animal;

c) waiting for a time interval following step (b) to permit the labeled antibody to concentrate at any cancerous site in the [subject] animal;

d) determining background level; and

e) detecting the labeled antibody in the [subject] animal, wherein detection of the labeled antibody above the background level at a site in the [subject] animal indicates the presence of a cancer at said site.

49. (Thrice Amended) A method for detecting cancer comprising:

a) administering plasma to [a subject] an animal;

b) waiting for a time interval following step (a);

c) administering an effective amount of a labeled antibody which specifically binds to C3b(i) to said [subject] animal;

d) waiting for a time interval following step (c) to permit the labeled antibody to concentrate at any cancerous site in the [subject] animal;

e) determining background level; and

f) detecting the labeled antibody in the [subject] animal, wherein detection of the labeled antibody above the background level at a site in the [subject] animal indicates the presence of a cancer at said site.

50. (Thrice Amended) A method for detecting cancer in [a subject] an animal, comprising imaging said [subject] animal at a time interval after administrating sequentially to said [subject] animal plasma and an effective amount of a labeled antibody which specifically binds to C3b(i), said time interval being sufficient to permit the labeled antibody to concentrate at any cancerous site in said [subject] animal, wherein detection of the labeled antibody localized at a site in the [subject] animal indicates the presence of cancer at said site.

EXHIBIT B

PENDING CLAIMS
AS OF APRIL 22, 2001
IN U.S. PATENT APPLICATION SERIAL NO. 09/392,500
ATTORNEY DOCKET NO. 9426-019

20. A method for detecting cancer comprising:

a) administering to an animal an effective amount of a labeled antibody which specifically binds to C3b(i) or a labeled antibody which specifically binds to C3b(i) covalently linked to a second molecule;

b) waiting for a time interval following the administration to permit the labeled antibody to concentrate at any cancerous site in the animal;

c) determining background level;

d) detecting the labeled antibody at a site in the animal; and

e) determining that cancer is present at said site in the animal if the labeled antibody is detected above the background level at said site in the animal.

21. The method of Claim 20, 48 or 49 in which the animal is a human.

22. The method of Claim 20, 48, 49, 58 or 59 in which the labeled antibody is a monoclonal antibody.

23. The method of Claim 20, 48, 49, 58 or 59 in which the labeled antibody is a humanized antibody.

24. The method of Claim 20, 48, 49, 58 or 59 in which the labeled antibody is labeled with a radioisotope.

26. The method of Claim 20, 48 or 58 in which time interval is 6 hours to 48 hours.

27. The method of Claim 20, 48, 49, 58 or 59 in which the labeled antibody is administered intravenously.

28. The method of Claim 20 which further comprises repeating steps (a) through (d) at monthly or yearly intervals.

29. A method for detecting cancer in an animal, comprising

(a) imaging said animal at a time interval after administering to said animal an effective amount of a labeled antibody which specifically binds to C3b(i) or a labeled antibody which specifically binds to C3b(i) covalently linked to a second molecule, said time interval being sufficient to permit the labeled antibody to concentrate at any cancerous site in said animal; and

(b) determining that cancer is present at a site in said animal if the labeled antibody is localized at said site in the animal.

30. The method of Claim 29 or 50 in which the animal is a human.

31. The method of Claim 29, 50 or 60 in which the labeled antibody is a monoclonal antibody.

32. The method of Claim 29, 50 or 60 in which the labeled antibody is a humanized antibody.

33. The method of Claim 29, 50 or 60 in which the labeled antibody is labeled with a radioisotope.

34. The method of Claim 29, 50 or 60 in which time interval is 6 hours to 48 hours.

48. A method for detecting cancer comprising:

a) administering plasma to an animal;

b) administering an effective amount of a labeled antibody which specifically binds to C3b(i) to said animal;

c) waiting for a time interval following step (b) to permit the labeled antibody to concentrate at any cancerous site in the animal;

d) determining background level; and

e) detecting the labeled antibody in the animal, wherein detection of the labeled antibody above the background level at a site in the animal indicates the presence of a cancer at said site.

49. A method for detecting cancer comprising:

a) administering plasma to an animal;

b) waiting for a time interval following step (a);

c) administering an effective amount of a labeled antibody which specifically binds to C3b(i) to said animal;

d) waiting for a time interval following step (c) to permit the labeled antibody to concentrate at any cancerous site in the animal;

e) determining background level; and

f) detecting the labeled antibody in the animal, wherein detection of the labeled antibody above the background level at a site in the animal indicates the presence of a cancer at said site.

50. A method for detecting cancer in an animal, comprising imaging said animal at a time interval after administrating sequentially to said animal plasma and an effective amount of a labeled antibody which specifically binds to C3b(i), said time interval being sufficient to permit the labeled antibody to concentrate at any cancerous site in said animal, wherein detection of the labeled antibody localized at a site in the animal indicates the presence of cancer at said site.

51. The method of Claim 20, 48, 49, 58 or 59 in which the labeled antibody is a human antibody.

52. The method of Claim 20, 50 or 60 in which the labeled antibody is a human antibody.

53. The method of Claim 48 or 49 in which the plasma is administered intravenously.

55. The method of Claim 48 or 58 which further comprises repeating steps (a) through (e) at monthly intervals.

56. The method of Claim 49 or 59 which further comprises repeating steps (a) through (f) at monthly or yearly intervals.

58. A method for detecting cancer comprising:

a) administering one or more IgM antibodies known to bind to improperly glycosylated cancer cells to a subject;

b) administering an effective amount of a labeled antibody which specifically binds to C3b(i) to said subject;

c) waiting for a time interval following step (b) to permit the labeled antibody to concentrate at any cancerous site in the subject;

d) determining background level; and

e) detecting the labeled antibody in the subject, wherein detection of the labeled antibody above the background level at a site in the subject indicates the presence of a cancer at said site.

59. A method for detecting cancer comprising:

a) administering one or more IgM antibodies known to bind to improperly glycosylated cancer cells to a subject;

b) waiting for a time interval following step (a);

c) administering an effective amount of a labeled antibody which specifically binds to C3b(i) to said subject;

d) waiting for a time interval following step (c) to permit the labeled antibody to concentrate at any cancerous site in the subject;

e) determining background level; and

f) detecting the labeled antibody in the subject, wherein detection of the labeled antibody above the background level at a site in the subject indicates the presence of a cancer at said site.

60. A method for detecting cancer in a subject, comprising imaging said subject at a time interval after administrating sequentially to said subject one or more IgM

antibodies known to bind to improperly glycosylated cancer cells and an effective amount of a labeled antibody which specifically binds to C3b(i), said time interval being sufficient to permit the labeled antibody to concentrate at any cancerous site in said subject, wherein detection of the labeled antibody localized at a site in the subject indicates the presence of cancer at said site.

61. The method of Claim 58 or 59 in which the IgM antibodies known to bind to improperly glycosylated cancer cells are administered intravenously.

62. The method of Claim 58, 59 or 60 in which the subject is a human.